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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,838	03/30/2004	Theoharis C. Theoharides	2003133.125US10	3057

23483 7590 10/02/2008

WILMERHALE/BOSTON
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BOSTON, MA 02109

EXAMINER
WANG, SHENGJUN

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
10/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/811,838	THEOHARIDES, THEOHARIS C.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-52* is/are pending in the application.

4a) Of the above claim(s) *45-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-44 and 49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted June 30, 2008 is acknowledged.

Double Patenting Rejections

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 40, 43 and 49-51are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 6,635,625; claim 1 of

U.S. Patent 6,645,482; claim 1 of U.S. Patent 6,624,148; claim 1 of U.S. Patent 6,641,806, claims 1-13 of U.S. Patent 6,984667; and claims 1 and 2 of U.S. Patent 7,115,278, in view of Widyarini. Et al. and High et al. (US 2002/0028779). The patents claim an anti-inflammatory composition comprising proteoglycan (chondroitin), flavonoid, and olive kernel extract, The patent do not expressly claim the employment of isoflavonoid, such as phenoxodiol, and/or genistein.

3. However, Widyarini et al. teaches that isoflavonoids, such as phenoxodiol (dehydroequol), and genistein, are potent anti-inflammatory agents. See, particularly, the abstract. High et al. teaches that genistein is known to have anti-inflammatory activity. See, particularly, paragraphs 0019, 0020 and 0041.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate an isoflavonoid, such as phenoxodiol.

It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

4. Claims 41, 42, and 44 and 52are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 6,635,625, in view of Widyarini, and High et al. for reasons set forth above and in further view of Ip et al.

5. '625 do not expressly claim tamoxifen.

6. However, the composition in '625 is for treatment of inflammatory condition in prostate, and Ip discloses that Tamoxifen is known to be useful for treatment of prostate cancer. See, particularly, the abstract.

7. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made, to further incorporate tamoxifen in the composition for treatment of prostate cancer patients who have inflammatory conditions.

8. One of ordinary skilled in the art would have been motivated to incorporate tamoxifen within the composition for treatment of prostate cancer because the composition is useful for treatment of inflammatory condition in prostate and tamoxifen is known to be useful for treatment of prostate cancer.

9. Claims 40, 43 and 49-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 40 of copending Application No. 10.610,909; in view of Widyarini et al. and High et al. The patents claims an anti-inflammatory composition comprising proteoglycan (chondroitin), flavonoid, and olive kernel extract, '909 does not expressly claim the employment of isoflavonoid, such as phenoxodiol.

10. However, Widyarini et al. teaches that isoflavonoids, such as phenoxodiol (dehydroequol), and genistein, are potent anti-inflammatory agents. High et al. teaches that genistein is known to have anti-inflammatory activity. See, particularly, paragraphs 0019, 0020 and 0041.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate an isoflavonoid, such as phenoxodiol.

It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

11. This is a provisional obviousness-type double patenting rejection.

Claim Rejections 35 U.S.C. 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40,43, 49-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of inflammatory components of a hormonally-dependent cancer, does not reasonably provide enablement for the treatment of the cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claims, as amended, extend the scope of treatment of hormonally dependent cancers from treatment of inflammatory components of the cancers. It is well understood in the art of cancer therapy that treatment of cancers is highly unpredictable. The particular agents cited herein are known to in the art for treatment of inflammatory conditions, but are not clearly indicated as useful for treatment of cancer, particularly the components other than inflammation. The application provide no working example or guidance and direction as to how these agents would be useful against cancer, other than as an anti-inflammatory agent. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The claimed composition intended for treatment of all components of hormonally dependent cancer, one of ordinary skill in the art would have to perform a undue experimentation to explore the claimed scope, without an insurance of success.

Claim Rejections 35 U.S.C. 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 40, 43 and 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Florio (WO 0097/21434), in view of Singh et al. (US 5,858,371), Nobile et al. (US 4,265,823) (in light of Dr. Duke's phytochemical and ethnobotanical database), Widyarini. et al. and High et al. (US 2002/0028779).

15. Florio teaches a anti-inflammatory composition comprising chondroitin sulfate, polyunsaturated fatty acid. See, particularly, the abstract.

16. Florio does not teach expressly the employment of quercetin, olive kernel extract, and isoflavonoids, such as genistein and phenoxodiol.

17. However, Singh et al. disclosed that quercetin is known to have anti-inflammatory activity. See, particularly, col. 8, lines 25 to col. 10, line 51. Noblie et al. (US 4, 265, 823) disclosed that estrole is a steroid which displayed anti-inflammatory properties (col. 10, lines 20-37). The claims state 'olive kernel extract'. Giving the phrase its broadest interpretation within reason, lacking any specific definition in the Instant specification, it is deemed that an 'olive kernel extract' may be a crude extract, or an isolated phytochemical from the olive kernel (seed). Estrone is a compound endogenous to olive kernel (see for example, Dr. Duke's Phytochemical and Ethnobotanical Database*, page 2 of internet print-out). Widyarini et al. teaches that isoflavonoids, such as phenoxodiol (dehydroequol), and genistein, are potent anti-inflammatory agents. See, particularly, the abstract. High et al. teaches that genistein is known to have anti-inflammatory activity. See, particularly, paragraphs 0019, 0020 and 0041.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a composition comprising chondroitin, a extract of olive kernel, such as estrole, a flavonoid, such as quercetin, and isoflavonoids, such as genistein and/or phenoxodiol.

A person of ordinary skill in the art would have been motivated to make a composition comprising chondroitin, a extract of olive kernel, such as estrone, a flavonoid, such as quercetin, and isoflavonoids, such as genistein and/or phenoxodiol because each of the ingredients are known to have anti-inflammatory activity. It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of known anti-inflammatory agents sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

> The evidence of record shows that the subject matter as claimed is a combination of known components selected for their known properties as anti-inflammatory agent. A claim which unites elements with no change in their respective anti-inflammatory properties to yield a predictable result is not patentable in the absence of secondary considerations.

For over a half century, the [Supreme] Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ...obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 [87 USPQ 303] (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

KSR Int'l v. Teleflex Inc., 82 USPQ2d 1385, 1395 (2007).

Thus, one of ordinary skill in the art would have had a reasonable expectation that the combination of these compounds would have been additively beneficial in treating any inflammatory condition including those conditions in prostate.

Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re AIler, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. Although the prior art did not specifically disclose the amounts of each constituent as in claim 42, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations of components because concentration is an art-recognized result-effective variable which would have been routinely determined and optimized in the pharmaceutical art. Furthermore, it is well settled that the "intended use" of a product or composition will not further limit claims drawn to a product or composition. See, e.g., In re Hack 114 USPQ 161.

18. Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above cited references before him.

19. Claims 41, 42 and 44 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Florio (WO 0097/21434), in view of Singh et al. (US 5,858,371), Nobile et al. (US 4,265,823) (in light of Dr. Duke's phytochemical and ethnobotanical database), Widyarini. et al. and High et al. (US 2002/0028779) for reasons set forth above and in further view of Ip et al.

20. The cited reference do not teach expressly the employment of tamoxifen.

21. However, Ip discloses that Tamoxifen is known to be useful for treatment of prostate cancer. See, particularly, the abstract.

22. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made, to further incorporate tamoxifen in the composition for treatment of prostate cancer patients who have inflammatory conditions.

One of ordinary skilled in the art would have been motivated to incorporate tamoxifen within the composition for treatment of prostate cancer because the composition is useful for treatment of inflammatory condition in prostate and tamoxifen is known to be useful for treatment of prostate cancer. The evidence of record shows that the subject matter as claimed is a combination of known components selected for their known properties as anti-inflammatory agents and chemotherapeutic agent. A claim which unites elements with no change in their respective properties to yield a predictable result is not patentable in the absence of secondary considerations.

For over a half century, the [Supreme] Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ...obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 [87 USPQ 303] (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

KSR Int'l v. Teleflex Inc., 82 USPQ2d 1385, 1395 (2007).

Response to the Arguments

Applicants' amendments and remarks submitted June 30, 2008 have been fully considered, but are not persuasive.

Regarding the double patenting rejections, applicants contend that the rejection merely makes a conclusive statement as there is not particular reasons to combine the issued patents and Widarini reference. Specifically, applicants argue that the intended inflammatory disorder in the issued patents are different from the inflammatory disorder disclosed by Widarini and High et al. The examiner respectfully disagrees.

23. First, In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Widyarini et al. teaches that isoflavonoids, such as phenoxodiol (dehydroequol), and genistein, are potent anti-inflammatory agents. Widyarini reveals that isoflavones are known in the art to have significant antioxidant, estrogenic and tyrosine kinase inhibitory activity. Widyarini shows that those isoflavones are useful against inflammation. High et al. teaches that genistein is known to have anti-inflammatory activity and are useful against a variety of diseases with distinct underline etiologies, from arthritis, to stroke, to cancer. (see, paragraphes [0050] to [0052]). Therefore, considering the cited references as a whole, one of ordinary skill in the art would have reasonably expected that the isoflavones herein be useful as anti-inflammatory agents in any of the anti-inflammatory compositions in the issued patents.

24. In response to applicant's argument that the references teach different intended use for the anti-inflammatory agents, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability

when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

25. As to the obvious rejections under 35 U.S.C. 103, the examiner again maintains that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Widyarini et al. teaches that isoflavonoids, such as phenoxodiol (dehydroequol), and genistein, are potent anti-inflammatory agents. Widyarini reveals that isoflavones are known in the art to have significant antioxidant, estrogenic and tyrosine kinase inhibitory activity. Widyarini shows that those isoflavones are useful against inflammation. High et al. teaches that genistein is known to have anti-inflammatory activity and are useful against a variety of diseases with distinct underline etiologies, from arthritis, to stroke, to cancer. (see, paragraphs [0050] to [0052]). Therefore, considering the cited references as a whole, one of ordinary skill in the art would have reasonably expected that the isoflavones herein be useful as anti-inflammatory agents in any of the anti-inflammatory compositions in the issued patents.

Further, it is noted that the claimed composition is for treatment of (inflammatory components of) hormonally-dependent cancer, not for arthritis. Furthermore, the cited references as a whole have shown that each and every active agents recited in claimed composition is known anti-inflammatory agent, the combination of them would have been obvious for reasons set forth in In re Kerkhoven, 205 USPQ 1069.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617